

remission) are known, among diseased tissue samples that have been subjected to different treatment regimes include e.g., chemotherapy, antisense RNA, etc. (Emphasis added).

Thus, Applicant has not amended these claims. If Applicant has misunderstood the Examiner's rejection, Applicant offers to amend the claims based upon further clarification of the rejection from the Examiner.

Regarding the Examiner's rejection in paragraph K, the Examiner stated that these claims fail to recite a necessary step of "averaging IDEF values." Applicant suspects that the Examiner is referring to "IDIF" values described in the specification. Applicant notes that claims 10 and 34 currently recite the averaging of IDIF values as described by the Examiner using the language:

"... determining an expression level of said selected expressed sequence to be an average of said differences. (Emphasis added).

Thus, Applicant has not amended these claims. If Applicant has misunderstood the Examiner's rejection, Applicant offers to amend the claims based upon further clarification or the rejection from the Examiner.

Applicant adds new claim 49 directed to providing a tactile indication to the user via the mouse, or other pointing device when a cursor is placed over a particular mark. The tactile indication can be in proportion to the expression level of the gene corresponding to the mark. Antecedent basis lies at page 13, lines 13-15.

Applicant adds new claim 50, directed to providing an aural indication to the user via the mouse, or other pointing device when a cursor is placed over a particular mark. The aural indication can indicate the expression level of the gene corresponding to the mark. Antecedent basis lies at page 13, lines 5-7.

Applicant adds new claim 51, directed to obtaining information from an internet based resource about a selected expressed sequence corresponding to said mark. The internet based resource can be a web site having GenBank information and the like. Antecedent basis lies at page 14, lines 1-3.

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Applicant adds new claim 52, directed to receiving from the user a selection of at least two of a plurality of marks and displaying information about genes corresponding to the user's selection. Antecedent basis lies at page 13, lines 29-32.

REJECTIONS UNDER 35 U.S.C. § 102(B)

The Examiner rejected claims 1-5, 20, 21 and 23 under 35 U.S.C. § 102(b) as being unpatentable over Zhao et. al. (Gene Vol. 156 pp. 207-213 1995). Zhao is cited as teaching a bioimaging analyzer that compares profiles of a multiplicity of genes simultaneously.

Zhao discusses a method for analyzing large numbers of cDNA plasmids from brain tissue. The Zhao method includes preparing a filter using cDNA plasmids isolated from a brain tissue sample. Zhao purified the plasmids and grided them onto a nylon membrane filter using a robot. Then, Zhao constructed probes on the filter from purified poly(A)+ RNA, again from brain tissue. Zhao then hybridized tissue samples with the filter. Then, using a Bioimaging Analyzer and an automatic quantification program, Zhao analyzed the amount of radioactivity existing at each of the probes and performed a data analysis as illustrated by a series of graphs in Fig. 3, page 211. Finally, Zhao performed sequence analysis for clones of interest. Thus, at the time of producing the graph, Zhao did not know the sequence or other characteristics of the cDNA sequences used as probes. It is only after he has displayed expression levels in the graph that he proposes to conduct experiments to determine the sequence of particular probes. The Examiner views Zhao's process as anticipating claims 1-5, 20, 21 and 23.

This rejection is moot in view of the claim amendment to recite the steps of receiving an input of a user's selection of a particular mark on a graph of expressed sequences and in response to this user input, displaying information about the selected expressed sequence.

Further, Zhao's method does not disclose the providing of a display of identification information about expressed sequences responsive to user selection. This could not be done with Zhao's method, since he performed the sequence analysis after graphing the

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expression levels at the probes--he did not have the sequence information to display at the time he made the graph. As shown in Fig. 3 of Zhao, the graph of Zhao's experimental results consists only of multiple data points. Zhao's goal was not to display information about particular genes, but rather to display results of an experiment. Thus, Zhao's graph of experimental results does not teach, nor even suggest, the visualization techniques provided by the methods, systems and computer programs of the present invention.

For at least these reasons, withdrawal of the rejection is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 103(A)

The Examiner rejected claims 25-29, 44, 45 and 48 under 35 U.S.C. § 103(a) as being unpatentable over Zhao et. al. (Gene Vol. 156 pp. 207-213 1995). Again, Zhao is cited as teaching a bioimaging analyzer that compares profiles of a multiplicity of genes simultaneously. The Examiner states that Zhao's expression profiles were illustrated on graphs by comparing the scores from two tissue samples using Microsoft Excel on a Macintosh personal computer. A mark for each gene is positioned relative to the expression levels in the two different samples. The Examiner acknowledges that Zhao does not teach implementing his system using computer code, but then argues that one of ordinary skill in the art would use Microsoft Excel to generate Zhao's graphs. The Examiner also argued that, in the alternative, one of ordinary skill in the art would have been motivated to "implement the Microsoft Excel program in code format to display the expression level in order to analyze various data inputs from various samples on different platforms."

This rejection is respectfully traversed as it applies to the presently claimed invention.

Zhao does not disclose, nor suggest, receiving user input indicating a particular mark in order to provide the user with information about the gene associated with the mark. Indeed, there would be no purpose in providing a user with such information in Zhao's method, because Zhao's method was performed using cDNA probes of unknown sequence for which he had no available information to display, not to providing a multi-purpose gene data base user interface. By contrast, the present invention provides a full function user interface

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for visualizing expression sequence information. Methods, systems and computer programs of the present invention can provide the user with useful information for visualizing the analysis of expression sequences. For example, the present invention provides for display of identification information, such as a GenBank accession number. Further, in some embodiments, the user can encircle multiple marks and obtain a list of information for all genes corresponding to the selected marks. Yet further, embodiments of the present invention can provide non-visual indications of expression level, such as tactile sensations, through a special mouse or pointing device, aural (sound) indications, and the like. Still further, some embodiments of the present invention can obtain information about genes using internet based resources, such as web pages and the like.

In sum, the present invention provides significant advances over the state of the art in tools for working with expression sequence analysis.

For at least these reasons, withdrawal of the rejection is respectfully requested.

The Examiner rejected claims 19 and 43 under 35 U.S.C. § 103(a) as being unpatentable over Zhao et. al. (Gene Vol. 156 pp. 207-213 1995). Again, Zhao is cited as teaching a bioimaging analyzer that compares profiles of a multiplicity of genes simultaneously. The Examiner admits that Zhao does not teach the use of a third axis. The Examiner argues that one of ordinary skill in the art would have been motivated to apply a third axis to Zhao in order to compare the expression level in a third sample.

Applicant respectfully traverses this rejection.

There is nothing in Zhao that suggests that more than two tissue samples would ever need to be displayed in a three dimensional display. Further, the displaying of information in a three dimensional format requires more than the simple addition of a third axis suggested by the Examiner. Three dimensional graphs can be difficult for people to comprehend. Gene expression sequence information can be difficult for users to grasp if not displayed clearly. Thus the present invention is not as easily conceived as the Examiner suggests. Rather, the Applicants had to fashion a display mechanism that would make three dimensional display of expression levels understandable to a user. This "human factoring" is neither taught nor suggested by Zhao's graph of experimental results.

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For at least these reasons, withdrawal of the rejection is respectfully requested.


The Examiner rejected claims 6-18 and 30-42 under 35 U.S.C. § 103(a) as being unpatentable over Lockhart et. al. (WO97/27317) in view of Zhao et. al. (Gene Vol. 156 pp. 207-213 1995). Lockhart is cited as teaching a method for detecting expression levels between two or more samples. The Examiner admits that Lockhart does not teach presenting expression level information by displaying a first axis representing the expression level in a first sample, displaying a second axis representing the expression level in the second sample and displaying a mark relative to the two axes. The Examiner again cites Zhao as teaching a bioimaging analyzer that compares profiles of a multiplicity of genes simultaneously. The Examiner then states that it "would have been prima facie obvious to construct a graph with an axis representing the gene expression in one sample and another axis representing the gene expression in a second sample in order to compare the differential gene expression between the samples."

Applicant respectfully traverses this rejection.

The combination of Lockhart and Zhao does not disclose, nor suggest, the gene visualization method, system and computer code of the present invention. Accordingly, all of the cited references suffer from essentially the same defect. None of the references discloses nor suggests receiving user input indicating a particular mark, or series of marks, in order to provide the user with information about the gene associated with the mark.

For at least these reasons, withdrawal of the rejection is respectfully requested.

The Examiner rejected claims 22, 24 and 46 under 35 U.S.C. § 103(a) as being unpatentable over Zhao et. al. in view of Beattie (U.S. 5,843,767). Beattie is cited as teaching the use of protein probes such as antibodies in an hybridization array. The Examiner again cites Zhao as teaching a bioimaging analyzer that compares profiles of a multiplicity of genes simultaneously. The Examiner admits that Zhao does not teach the use of protein polymers. The Examiner argues that one of ordinary skill in the art would have applied Beattie's teaching of protein probes to Zhao's expression display in order to compare the expression levels of translated protein between two samples.



Applicant respectfully traverses this rejection.

The combination of Beattie and Zhao does not disclose, nor suggest, the gene visualization method, system and computer code of the present invention. Accordingly, all of the cited references suffer from essentially the same defect. None of the references discloses nor suggests receiving user input indicating a particular mark, or series of marks, in order to provide the user with information about the gene associated with the mark.

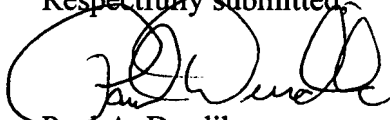
For at least these reasons, withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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